Mushroom compost worker's lung

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Summary

This study draws attention to difficulties in the diagnosis and the understanding of the mechanism of action of mushroom compost worker's lung. Descriptions are given of 4 workers in one factory who developed acute respiratory failure within a 6-month period; 13 others who were unaffected were also studied. Serological investigation appears to be largely unhelpful, and the evidence against the condition being included amongst the extrinsic allergic alveolitides is discussed. A detailed clinical and occupational history is essential for diagnosis.

Introduction

Respiratory disease amongst mushroom workers was first described in 1959 by Bringhurst *et al.*[1]. The first report from the UK by Sakula[2] introduced the term 'mushroom worker's lung' and emphasized clinical similarities with farmer's lung. Two further British reports have since appeared[3,4] and this condition is now generally presumed to be an example of extrinsic allergic alveolitis[5-7].

This paper includes descriptions of the acute illnesses of 4 young or middle-aged men recently employed in the bagging shed of a Cambridgeshire factory which produces compost for mushroom cultivation. This shed is a Dutch barn where the finished compost is collected together, then dropped from an overhead shute into polythene bags for sale to mushroom farms. All the patients presented within six months; the factory had been operating for many years without previous cases and we learnt of no recent changes in the process of compost production.

Case reports

Case 1: A 21-year-old man was admitted to another hospital with a two-week history of cough, breathlessness, headache and malaise four weeks after starting work at the factory. He was pyrexial (39°C), tachypnoeic and centrally cyanosed. Late inspiratory crackles were heard over both lungs. Chest X-ray showed diffuse bilateral micronodular shadows.

Atypical pneumonia was diagnosed. He was treated with erythromycin and recovered over two weeks. The X-ray cleared and there was a rise in complement-fixing antibody titre to *Mycoplasma pneumoniae* from less than 1 in 8 on admission to 1 in 64 ten days later.

He returned to work two weeks later, and within six hours all his symptoms and signs recurred. He was profoundly hypoxaemic (Pao_2 breathing room air 3.8 kPa). Chest X-ray (Figure 1) showed diffuse bilateral micronodular shadows and tests of lung function revealed reduced lung volumes and a low gas transfer for carbon monoxide (TLCO) (Table 1). Haemoglobin was 16.4 g/dl, white cell count 13.2×10^9/l (normal differential) and ESR 10 mm/h.

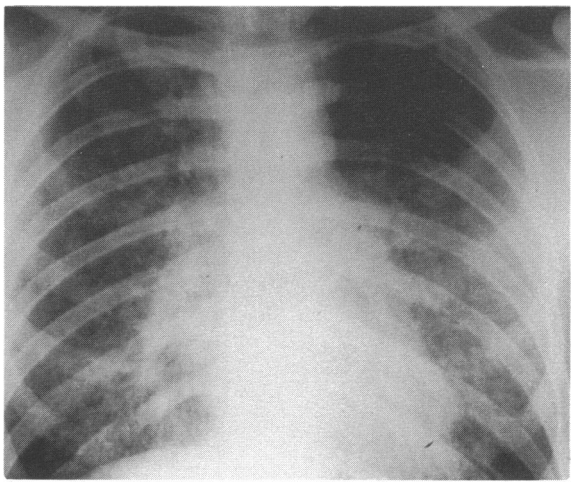

Figure 1. Chest radiograph of Case 1 showing diffuse bilateral micronodular shadows

A diagnosis of mushroom compost worker's lung was made and treatment commenced with 60% oxygen and oral prednisolone (60 mg daily). All symptoms and signs disappeared in two days. Chest X-ray cleared in a week. The titre of antibodies to *M. pneumoniae* was 1 in 16 on admission, and did not change when measured at fortnightly intervals over the next two months. The prednisolone dose was reduced over three weeks, then stopped. He remained well without symptoms. Over the next six months lung volumes returned to normal, but the TLCO remained low.

Case 2: A 17-year-old man developed cough, breathlessness, shivers and joint pains one week after starting work. These symptoms persisted for four days, worsening each afternoon, reaching a peak in the late evening then improving by the following morning. He was pyrexial (38.5°C), tachypnoeic and centrally cyanosed. Late inspiratory crackles were heard over both lungs.

Breathing room air Pao_2 was 7.1 kPa. Chest X-ray showed diffuse bilateral micronodular shadows and lung function tests revealed reduced lung volumes and a low TLCO (Table 1). Haemoglobin was 13.6 g/dl, white cell count 7.6×10^9/l (normal differential) and ESR 39 mm/h.

All clinical and radiographic abnormalities resolved within 24 hours of starting treatment with oral prednisolone (60 mg daily). There was no rise in titre to *M. pneumoniae, Chlamydia psittaci, Legionella pneumophila*, influenza A and B and adenovirus. The dose of prednisolone was reduced

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Table 1. Results of lung function tests in patients at presentation, at six weeks and after six months

	FEV_1 (l)	FVC (l)	FEV_1/FVC	TLCO (ml/kPa/min)	Total lung capacity (l)
Case 1					
(Predicted)	(3.6–4.5)	(4.4–5.4)	(81–82)	(11.3–14.1)	(5.3–6.4)
Week 1	2.1	2.8	75	4.2	4.0
Week 6	2.8	3.9	71	6.4	4.8
Week 38	4.3	4.9	88	8.7	6.3
Case 2					
(Predicted)	(3.6–4.5)	(4.4–5.5)	(82–83)	(10.6–13.6)	(5.6–6.7)
Week 1	2.5	4.1	61	5.6	5.8
Week 6	5.0	6.5	76	10.2	6.6
Week 32	5.1	6.7	76	10.0	8.3
Case 3					
(Predicted)	(3.4–4.3)	(4.2–5.7)	(71–79)	(12.5–15.3)	(6.9–8.4)
Week 1	1.9	4.4	42	7.7	8.3
Week 6	3.2	5.3	59	11.2	8.0
Week 26	3.3	5.5	60	11.3	–
Case 4					
(Predicted)	(3.3–4.2)	(4.6–5.6)	(71–74)	(12.1–14.9)	(6.7–8.2)
Week 1	3.9	5.1	77	6.9	6.6
Week 6	4.4	5.6	77	8.6	8.0
Week 34	4.3	5.9	73	9.7	9.2

over two weeks, then stopped. He remained well without symptoms. By six weeks lung volumes were normal but even at six months the TLCO was low.

Case 3: A 46-year-old man who had smoked 20 cigarettes a day for many years developed breathlessness but no other symptoms two weeks after starting work. Late inspiratory crackles were heard over the lower lobes. Chest X-ray was normal. Lung function tests showed reduced lung volumes, severe airflow obstruction and a low TLCO (Table 1). Haemoglobin was 16.5 g/dl, white cell count 7.4×10^9/l (normal differential) and ESR 15 mm/h.

All symptoms and signs resolved within one week of starting oral prednisolone (30 mg daily). There was no rise in titre to *M. pneumoniae, C. psittaci, L. pneumophila*, influenza A and B and adenovirus.

The dose of prednisolone was reduced over three weeks, then stopped. By six weeks lung function tests showed improvement, but at six months mild airflow obstruction and a low TLCO persisted. Smoking-related emphysema may contribute to these persisting abnormalities.

Case 4: A 46-year-old non-smoker developed tiredness, aching limbs, sweats and dry cough four weeks after starting work. All his symptoms resolved during two weeks away from work but recurred within a day of his return. He took another week off. The symptoms resolved but again recurred on his first day back at work. At this time late inspiratory crackles were audible over the right upper chest. Chest X-ray showed patchy asymmetrical mid and lower zone shadowing. Breathing room air Pao_2 was 9.1 kPa. Lung function tests showed lung volumes within the predicted range but a low TLCO (Table 1). Haemoglobin was 16.2 g/dl, white cell count 6.0×10^9/l (normal differential) and ESR 58 mm/h. There was no rise in titres to *M. pneumoniae, C. psittaci, L. pneumophila*, influenza A and B and adenovirus.

At fibreoptic bronchoscopy the airways appeared normal. Bronchoalveolar lavage was performed and transbronchial biopsies taken from the middle and right lower lobes. Histological examination revealed intra-alveolar macrophages, mild swelling of alveolar walls and minimal interstitial round cell infiltration. No granulomas or fibrosis were seen (Figure 2). No IgG nor IgA was demonstrated with immunofluorescent stains. Neither bacteria nor fungi were seen; cultures proved sterile.

All symptoms resolved within one week of starting treatment with prednisolone (30 mg daily). Chest X-ray was normal one month later when the prednisolone was stopped. He remained well. Over six months there was a significant increase in lung volumes. TLCO also increased but remained below the predicted range (Table 1).

Survey of unaffected workers

The 13 asymptomatic men who were performing the same work at the factory were examined for evidence of subclinical disease. All were questioned about cigarette smoking and respiratory or systemic symptoms related to work. Forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) were measured in all 13, and the TLCO in 11.

Eight were smokers, 4 ex-smokers and one had never smoked. One young man with severe airflow obstruction had symptoms of longstanding, previously undiagnosed asthma, unrelated to work. The others had no symptoms. Excluding the man with asthma, all values for FEV_1, FVC and forced expiratory ratio ($FEV_1/FVC \times 100\%$) fell within the predicted range. All the TLCO values were greater than 70% of predicted.

Immunological findings

Only the unaffected worker with asthma proved atopic when prick-testing with common allergens was performed on all the patients and unaffected workers. Saline extracts of compost (0.5 g compost in

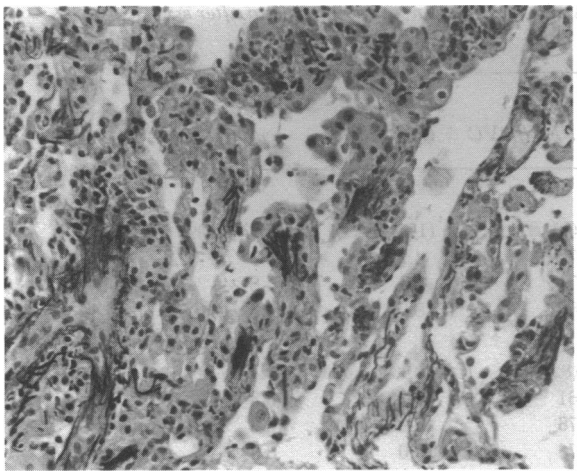

Figure 2. Transbronchial biopsy, Case 4, showing intra-alveolar macrophages, some mild swelling of alveolar walls with minimal interstitial round cell infiltration. (E1. VG × 420; reduced 61%)

5 ml of isotonic saline) and atmospheric dust from the bagging shed were prepared. Prick-testing with these extracts was negative in both patients and unaffected workers. Intradermal injection produced no reaction over 72 hours in 4 patients.

Antibodies against these extracts were sought in serum from patients and unaffected workers using double diffusion agar gel and ELISA techniques. None were found. Using double diffusion agar gel techniques, no antibodies were detected against *Micropolyspora faeni, Thermactinomyces vulgaris, Aspergillus fumigatus* and fowl antigens. Anti-nuclear factor, rheumatoid factor and organ-specific autoantibodies were not found in the serum of the patients.

Further investigations were performed in Case 4. There was no evidence of complement activation, serum C3 (266 mg/dl; normal range 60–80) and C4 (44 mg/dl; normal range 10–35) being elevated as part of an acute phase response. Serum concentrations of IgG, IgA and IgM were normal and there was no excess of circulating immune complexes (23%; normal range up to 24%). Lymphocytes comprised 23% of the total peripheral blood leukocyte count of 6.0×10^9/l, T and B cells being present in the expected proportions (73% and 3% respectively). The T helper/suppressor ratio of 2.5 was within the normal range. Cells obtained at bronchoalveolar lavage showed a greatly increased proportion of lymphocytes (40%) with increased neutrophils (19.5%) and eosinophils (12%)[8]; 90% of the lymphocytes were T cells and 4% B cells. The T helper/suppressor ratio was 2.3.

Discussion

The agent responsible for this condition is not known. It is generally thought to be a component of the compost used in mushroom cultivation[5–7], though there have in the past been claims of a direct role for mushrooms themselves[9]. Previous reports have described patients working on farms where both the preparation of compost and cultivation of mushrooms were carried out[2–4]. Our patients had no connection with mushrooms themselves, so we suggest that 'mushroom compost worker's lung' is a more accurate diagnostic term for this condition.

Our patients illustrate the different ways in which it may present. The first 2 developed severe breathlessness and marked systemic upset in association with diffuse micronodular shadows on chest X-ray, a restrictive ventilatory defect with gross impairment of gas exchange and biochemical evidence of acute respiratory failure. The third was breathless without constitutional upset, had a normal chest X-ray and severe airflow obstruction; nevertheless, there was evidence for interstitial lung disease from the late inspiratory crackles and low gas transfer which improved with treatment. The fourth patient had predominantly constitutional symptoms but the cough and crackles, together with the typical lung function abnormalities, abnormal chest X-ray and histological findings, confirmed interstitial lung disease.

The importance of obtaining the relevant occupational history in making this diagnosis cannot be overstated. With the first type of presentation, atypical pneumonia is likely to be misdiagnosed if it is overlooked. Our first patient nearly died when he returned to work because of this. A *Mycoplasma pneumoniae* infection seemed to have been confirmed by the greater than four-fold rise in titre of antibodies against this organism. Similar rises in titre against other organisms responsible for atypical pneumonias have been reported in pigeon-fancier's lung[10,11]. The mechanism is uncertain, but it makes it even more important that an occupational history is obtained.

The epidemiology of mushroom compost worker's lung, with sporadic outbreaks at one site after many uneventful years, suggests that the agent responsible is an occasional contaminant of incompletely pasteurized compost. A thermophilic fungus would seem most likely[12] but this has never been proven.

In the past this condition has usually been included amongst the extrinsic allergic alveolitides[5–7]. This has been based on radiological, physiological and serological evidence. The radiographic abnormality most widely recognized is diffuse bilateral micronodular shadowing[13], as in other examples of extrinsic allergic alveolitis[14], but patchy asymmetrical shadowing and even a normal X-ray[13], as in our third patient, may be found. The abnormalities of lung function in our patients and those previously reported[15,16] have typically been of 'stiff lungs' with a reduction in lung volumes and transfer factor. This is consistent with extrinsic allergic alveolitis[17]. A feature of several previous reports[15,18], also noted by us, is that the gas transfer remains low for many months, even when lung volumes have returned to normal. Marked airflow obstruction, as seen in our third patient, has not previously been recorded.

The serological evidence in support of this being an extrinsic allergic alveolitis is, however, unconvincing. The idea that antibodies may play a role in pathogenesis stems from Sakula's report[2] of precipitins against *Micropolyspora faeni* in the serum of one of his 4 patients and against *Thermactinomyces vulgaris* in that of another. Subsequent investigators have failed to identify any consistent serological abnormality in their patients. On the other hand, Moller *et al.*[19] showed that 55% of asymptomatic long-term employees at a mushroom factory had precipitins against *Micropolyspora faeni* in their serum. The presence of such precipitins is likely to reflect exposure to the organism and does not imply that they have any role in pathogenesis.

There is, indeed, no real evidence for any pathogenic humoral or cell-mediated immune reaction. Ours is the first report of bronchoalveolar lavage in

this condition. The increase in inflammatory cells, particularly lymphocytes, that we have found is consistent with the findings in extrinsic allergic alveolitis[20-22], but not specific for this. Histological examination of the lung in our fourth patient failed to reveal the granulomas characteristic of an acute extrinsic allergic alveolitis. This was also the case in the two previous histological studies[3,16].

In view of this lack of support for the immune reactions typical of extrinsic allergic alveolitis, other pathogenetic mechanisms should be considered. It was suggested in the original description[1] that there were similarities with silo filler's lung, a condition in which high concentrations of nitrogen dioxide evolved from silage cause an acute toxic pulmonary reaction[23]. There is, however, no evidence that nitrogen dioxide is generated from mushroom compost.

Emmanuel *et al.*[24] have reported an acute respiratory illness with marked systemic upset. Culture of lung biopsy from one patient yielded 5 different fungi. They considered the illness to be an effect of a fungal toxin and called it 'pulmonary mycotoxicosis'. Ours is the first report of culture of lung biopsy material in mushroom compost worker's lung. The negative findings do not support such a pathogenesis.

Some examples of humidifier fever are associated with contamination of air-conditioning systems by bacteria, fungi or protozoa[25] and an endotoxin-mediated pathogenesis has been proposed[26]. It has also been suggested that endotoxins may be responsible for sewage sludge disease[27] in which sewage disposal plant workers develop chills and malaise. *In vitro*, mouldy hay can activate complement via the alternate pathway[28] and it is argued that micro-organisms or their toxins may initiate these conditions[29,30] by this mechanism. A component or toxic product of mushroom compost could conceivably cause mushroom compost worker's lung in a similar way, but again there is no evidence available.

Whilst the pathogenesis remains to be established, mushroom compost worker's lung is of importance to the clinician as a potentially fatal pulmonary disease, easily confused with atypical pneumonia but requiring very different treatment. It will only be diagnosed if the relevant occupational history is obtained.

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